REMARKS

Reconsideration of the above-identified application is respectfully requested. Claims 30 and 32 are currently pending and under consideration.

Withdrawal of Objection to the Claims and Abstract and Rejections Under 35 U.S.C. § 112

Applicants thank the Examiner for withdrawing the objections to claims 32 and the abstract and the rejections of claims 31 and 32 under 35 U.S.C. § 112, first paragraph, in light of Applicant's previously submitted amendment.

Rejection Under 35 U.S.C. § 102(e)

Claims 30 and 32 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 5,622,852 (the '852 patent). More specifically, the Examiner asserts that the '852 patent teaches a monoclonal antibody to a mouse Bad polypeptide. The Examiner concludes that such antibodies would inherently bind to the polypeptide of SEQ ID NO:2, since the mouse Bad polypeptide is 75% similar to SEQ ID NO:2, from amino acid residues 1 to 168. Furthermore, the Examiner asserts that the '852 patent teaches monoclonal antibodies directed to the BH1 domain of a mouse Bad polypeptide, which would also inherently bind to the BH1 domain of a human Bad polypeptide, given the degree of sequence conservation between the described mouse and Bad polypeptides.

Applicants respectfully traverse this basis of rejection and submit that the Examiner has failed to establish a *prima facie* case of anticipation of the presently claimed invention by the '852 patent, since the '852 patent does not described antibodies that specifically bind to a human Bad polypeptide, and the Examiner has failed to demonstrate that the antibodies described in the '852 (which are specific for a mouse Bad polypeptide) would inherently bind to a human Bad polypeptide.

Contrary to the Examiner's assertion that the burden rests on Applicants to conclusively demonstrate that the antibodies described in the '852 patent bind to a human Bad polypeptide, it is clearly established under U.S. patent laws that the examiner bears the initial

burden of establishing that the subject matter of the presently claimed invention is inherently present in the'852 patent.

M.P.E.P §2112 provides that:

> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Ex parte Levy*, 17 USPQ2d 1461, 1464 (BPAI 1990) (emphasis in original).

Accordingly, Applicants submit that the burden remains with the PTO to supply the requisite basis in fact and/or technical reasoning, where, as Applicants have previously argued, mere conjecture on the part of the PTO does not suffice as a finding that the prior art reference contains a disclosure that anticipates the presently claimed invention. Furthermore, the PTO has offered no evidence making clear that "the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." (*Continental Can Co. USA v. Monsanto Co.*,948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (M.P.E.P. § 2131.01 (III)).

Indeed, Applicants submit that the skilled artisan, based upon established scientific principles, would clearly recognize that the antibodies described in the '852 patent do not necessarily bind to a human Bad polypeptide of SEQ ID NO:2. It is well known in the art that even a single amino acid change can effect the folding and immunogenic properties of a polypeptide. With regard to the immunogenic properties of related polypeptide, Houghten *et al.* (Vaccines, 1986, Edited by Fred Brown: Cold Spring Harbor Laboratory) teaches that changes and modifications of one or more amino acids in a polypeptide will alter antigenic determinants and therefore affect antibody binding (p.21). Indeed, Houghten *et al.* notes that "...combined effects of multiple changes in an antigenic determinant could result in a loss of [immunological] protection," and "a protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). Furthermore, Houghten *et al.*

enunciates the common understanding in the art when stating that point mutations at one key antigen residue could eliminate the ability of an antibody to recognize the altered antigen (p. 24).

In light of this clear understanding in the art, Applicants submit that the skilled artisan would certainly be of the opinion that antibodies to a mouse Bad polypeptide would not inherently or necessarily bind to a human Bad polypeptide, particularly given that the sequence homology between the two full length polypeptides is only approximately 75%, and the fact that two amino acid substitutions exist within the relatively small region of 24 amino acids constituting the BH1 domain. Applicants respectfully submit that the skilled artisan would, thus, have no basis for concluding that the presently claimed subject matter is *necessarily* coextensive in scope with any antibody disclosed in the '852 patent. Accordingly, the PTO has failed to meet its burden of establishing that the subject matter of the presently claimed invention is inherently present in the '852 patent.

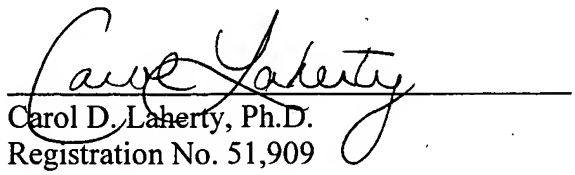
Applicants, therefore, submit that the PTO has failed to meet its burden of supplying extrinsic evidence to supplement the incomplete disclosure of the '852 patent, and that the PTO, therefore, cannot demonstrate that an antibody of the '852 patent *necessarily* must bind to a human Bad polypeptide or fragment thereof, as recited according to the instant claims. Accordingly, no *prima facie* case of anticipation under 35 U.S.C. §102(b) has been established, and Applicants respectfully request that the rejection be withdrawn.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all of the claims in the application are clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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